

Plaque profilings

Insights from the Culprit Plaques

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|| Big Leafs in CV Medicine

Statins and Anti-platelet Agents



HMGCo-A Reductase

P2Y₁₂ Receptor

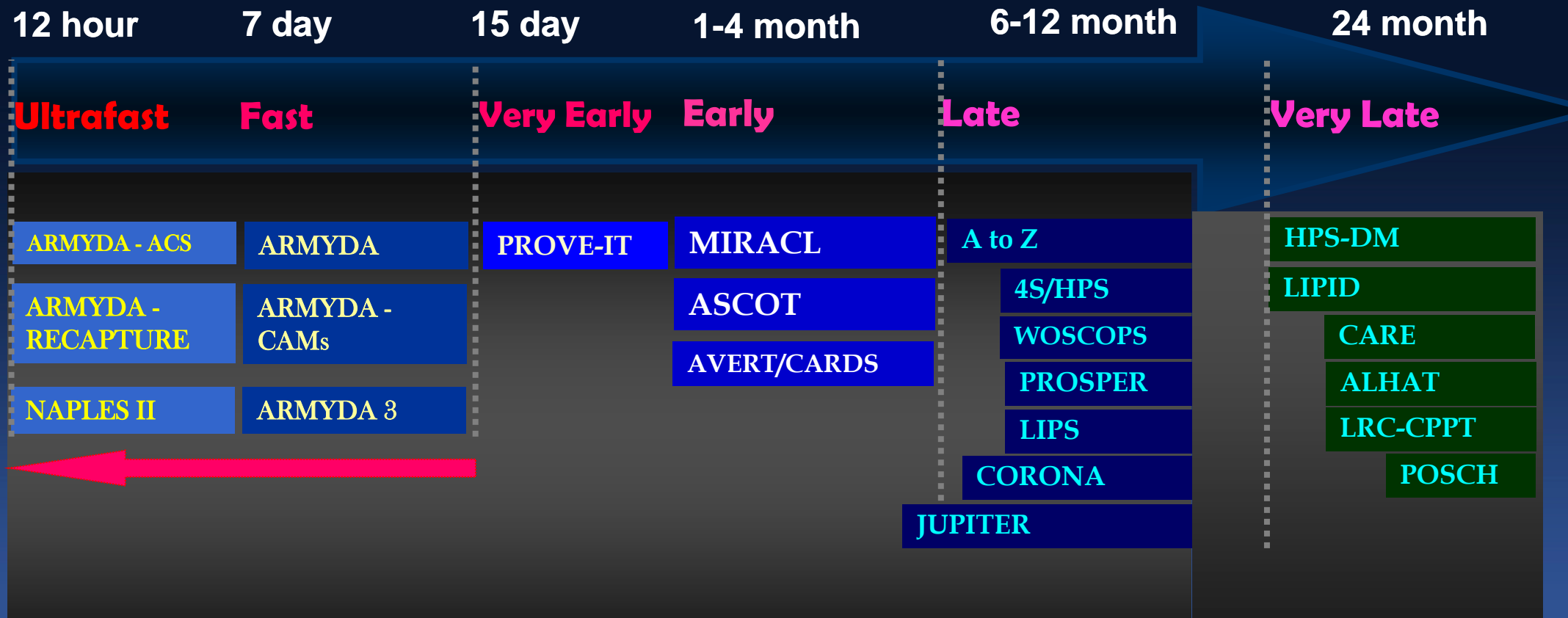
...the only proven medicine

Landmark Statin Trials

So Luxurious ...

Statin is an anti-atherosclerotic drug.

Rapid Effects of Statin Therapy



Mechanisms of early benefits are not fully understood.

Expression of HMG-CoAR in Human Coronary Plaques & Relationship to Plaque Destabilization

Heart 2011;97:715-20

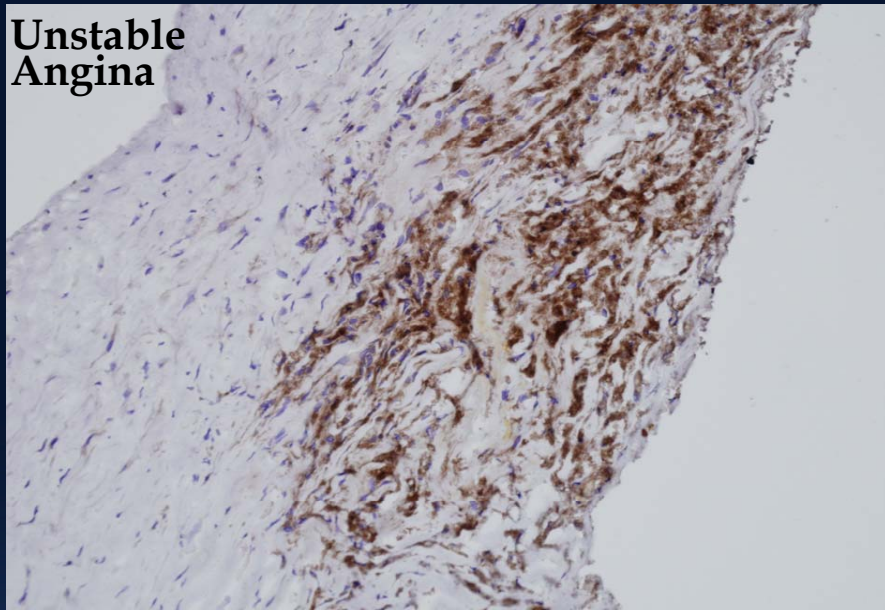
We investigated the expression of HMG-CoAR in coronary atherectomy tissues retrieved from 43 patients with unstable & stable angina, & examined the relationship of HMG-CoAR with plaque instability.

Immunohistochemistry

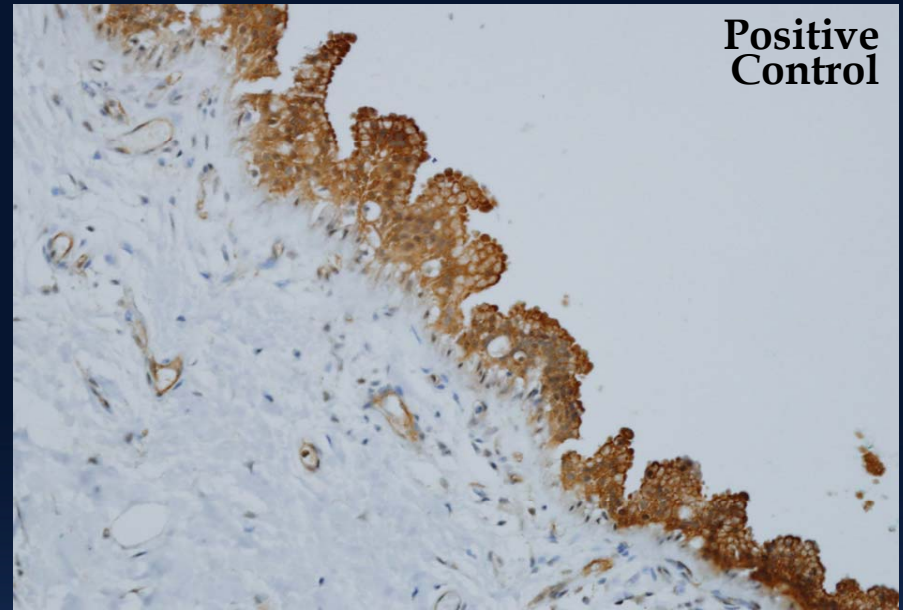
	Unstable angina (n=22)	Stable angina (n=21)	<i>p</i> - value
α -SM actin (%)	21.4 \pm 18.7	33.6 \pm 28.7	0.103
CD31 (%)	3.4 \pm 4.1	0.3 \pm 0.5	0.002
CD68 (%)	10.9 \pm 16.2	1.8 \pm 1.7	0.016
HMG-CoA R (%)	3.0 \pm 4.5	0.4 \pm 0.7	0.014

Data are shown as % positive area (immunostaining area/total plaque area \times 100).

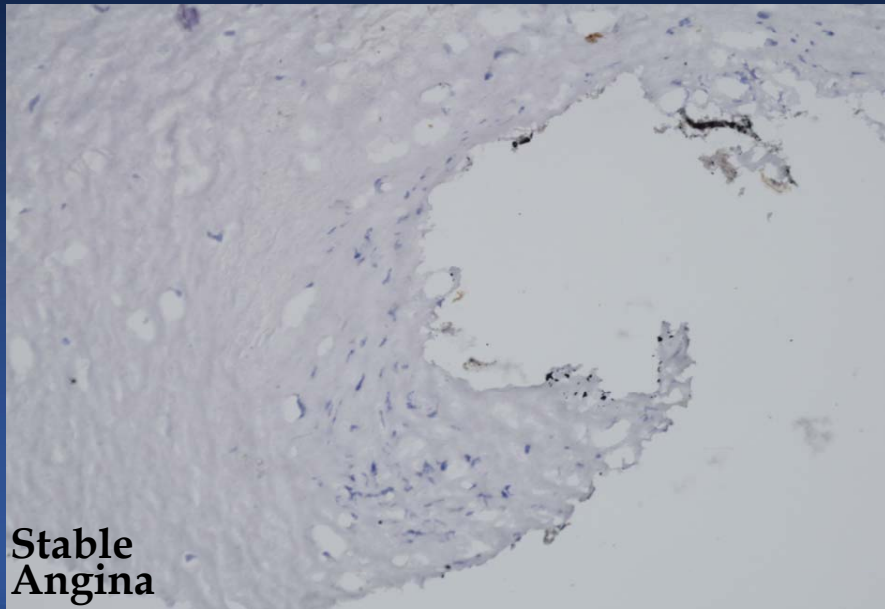
**Unstable
Angina**



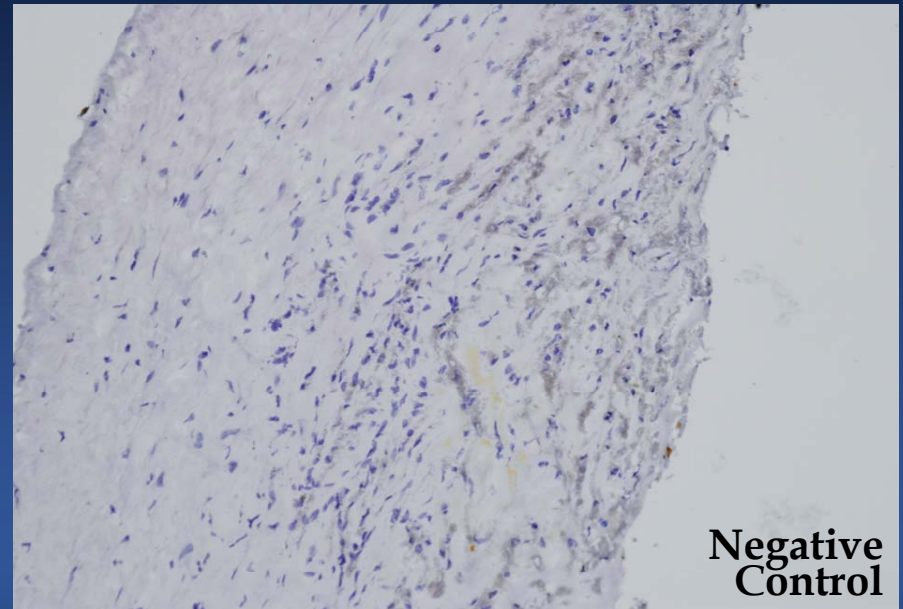
**Positive
Control**

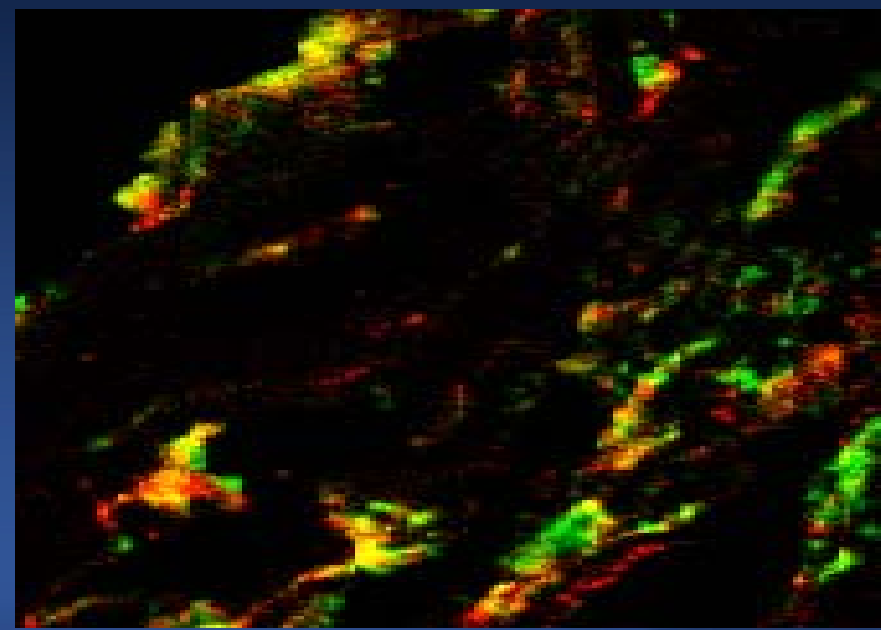
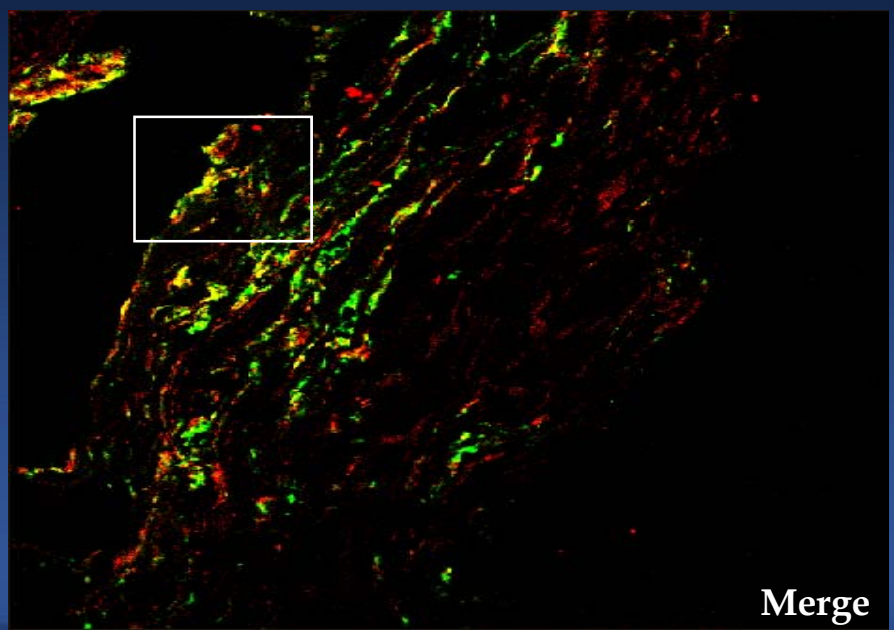
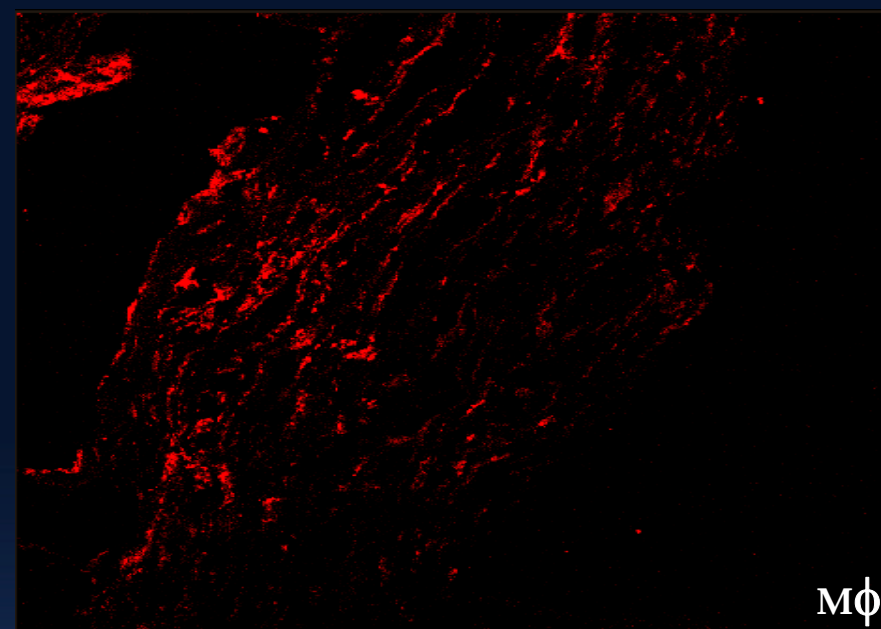
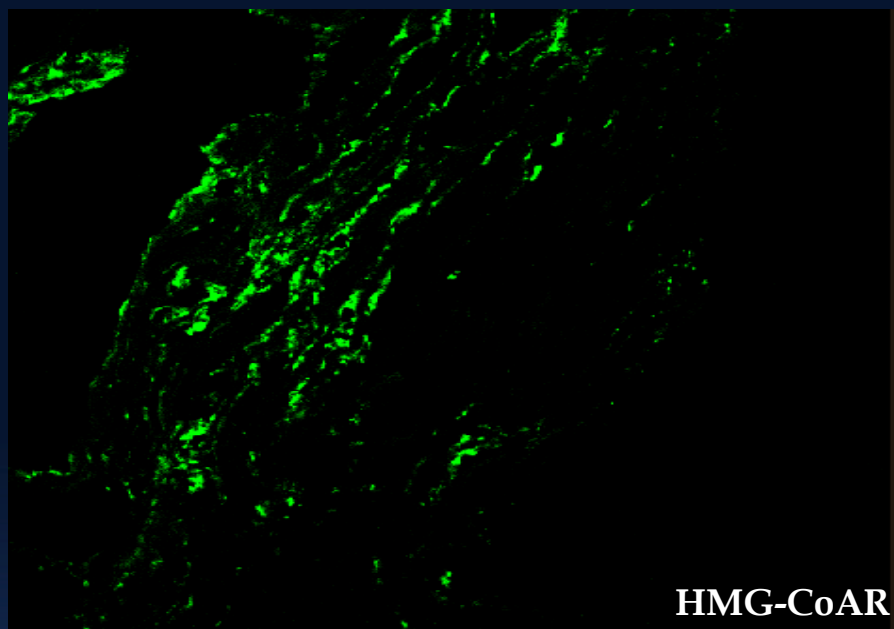


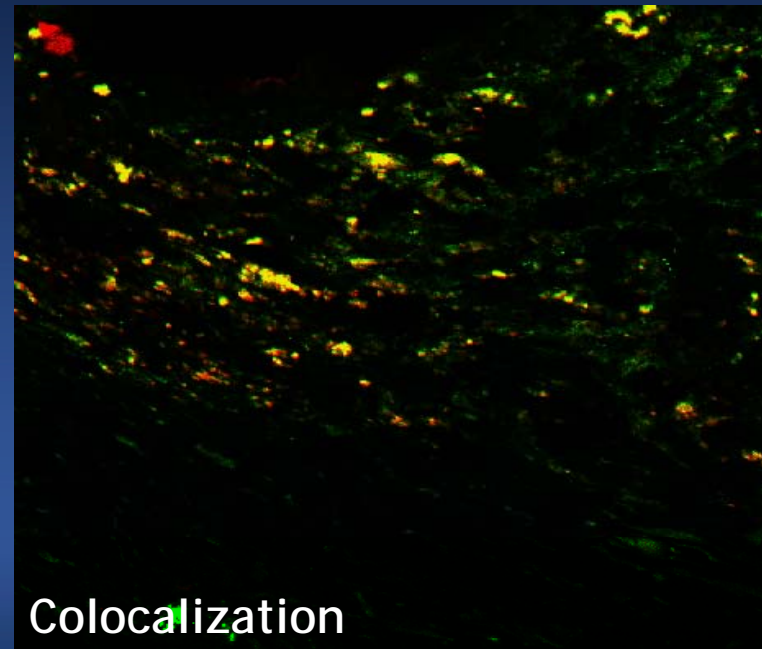
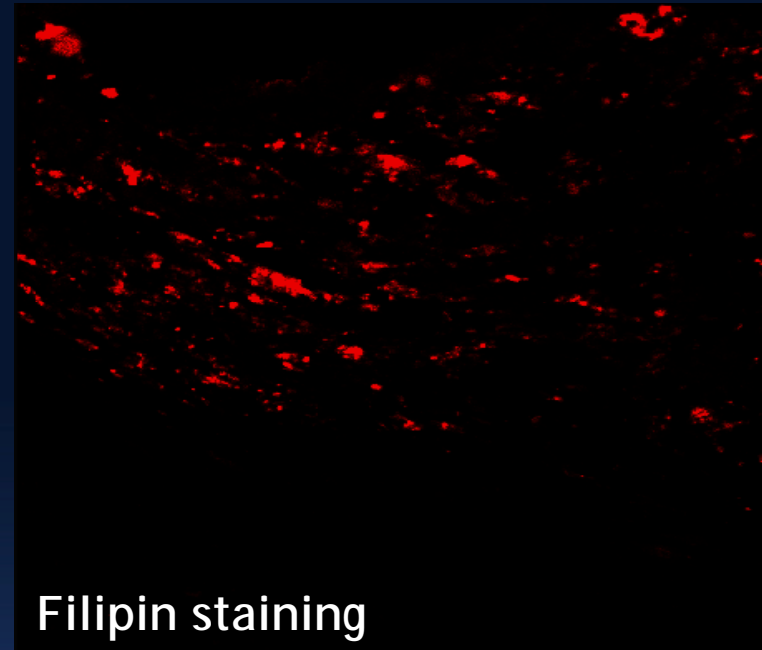
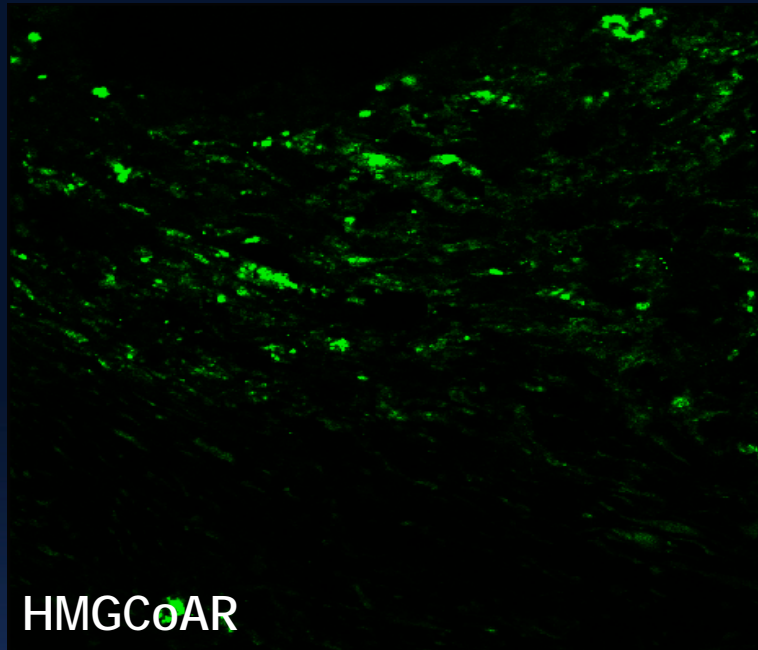
**Stable
Angina**



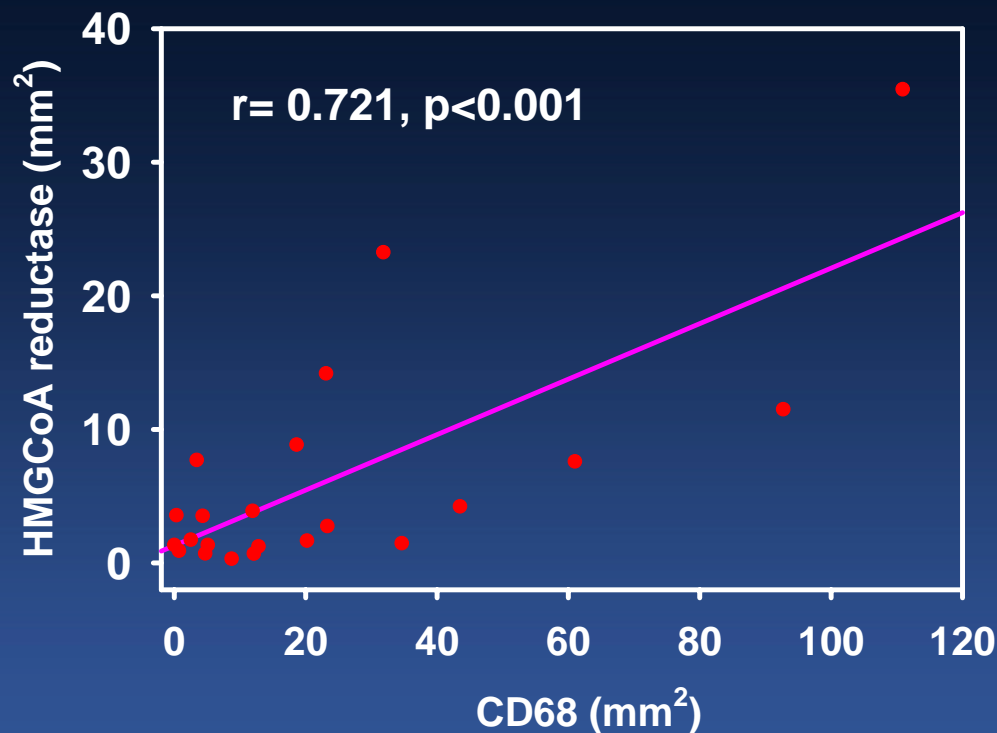
**Negative
Control**



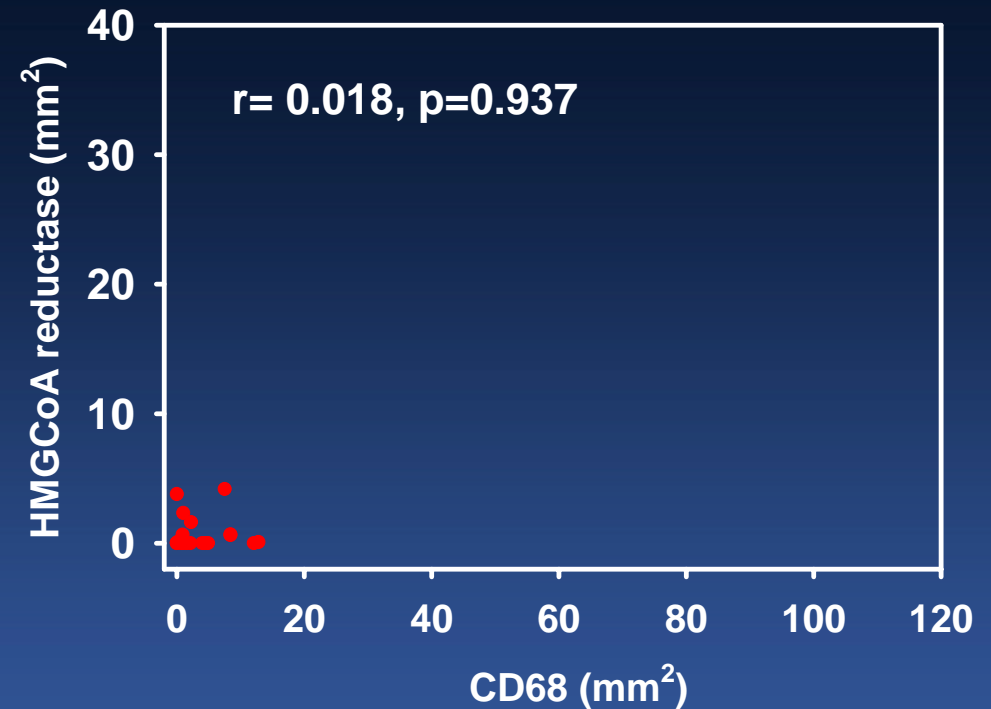




Relationship Between CD68-Positive Areas & HMG-CoA Reductase-Positive Areas (mm²)

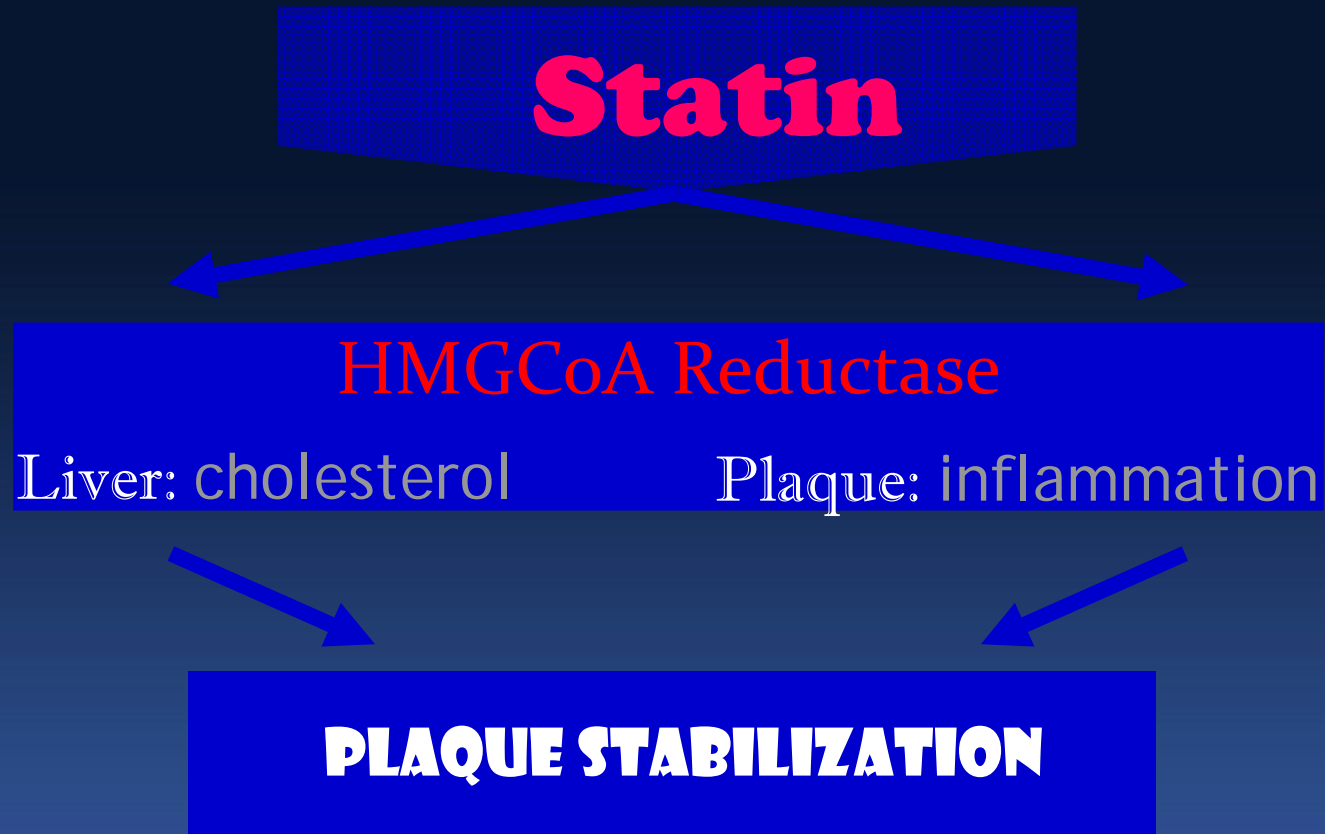


Unstable Angina



Stable Angina

Summary



These findings support a potential role of the HMG-CoAR in the pathogenesis of ACS, and may help explain the early benefits of statin therapy in patients with ACS.

|| Big Leafs in CV Medicine

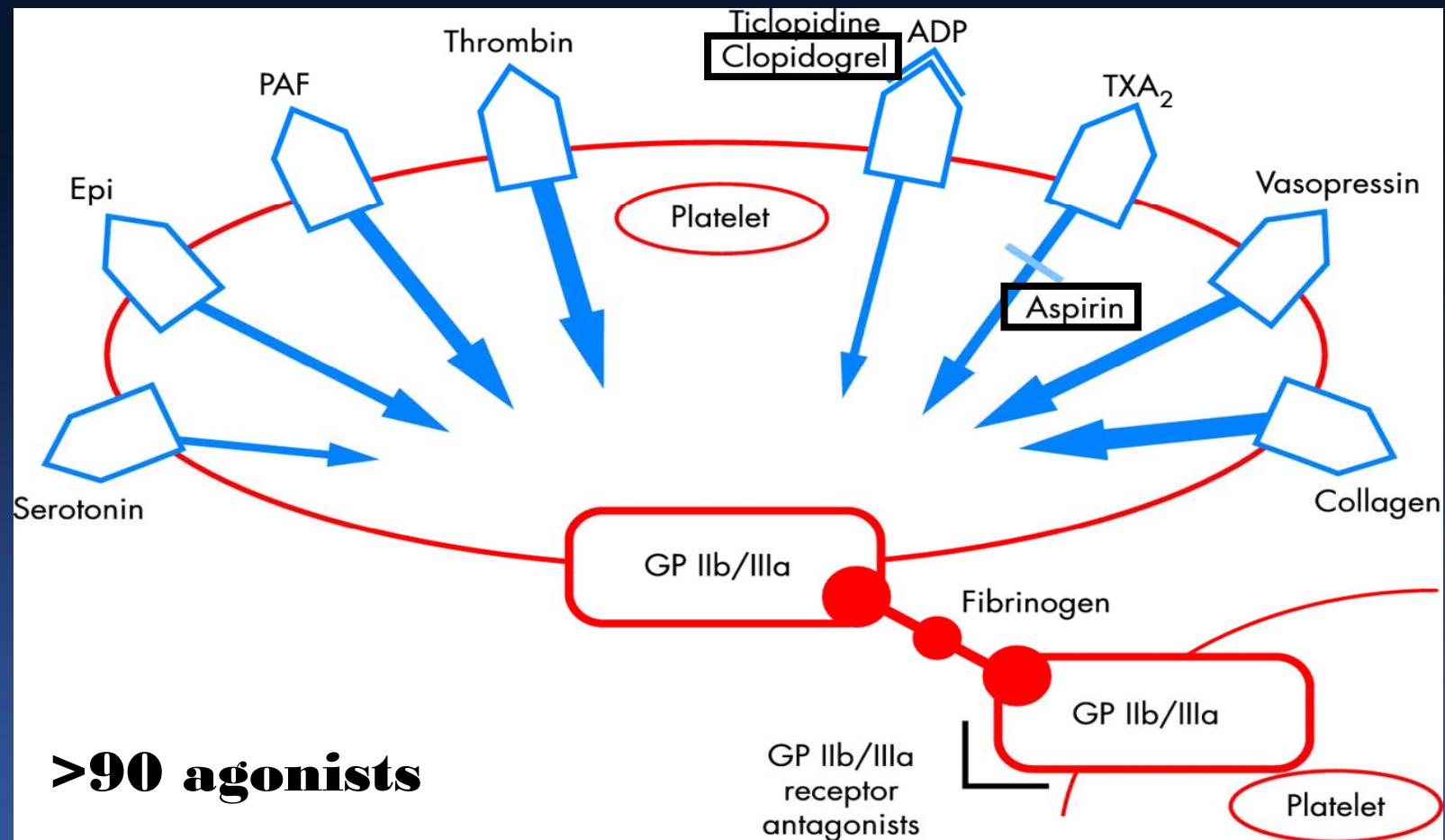
Statins and Anti-platelet Agents



HMGCo-A Reductase

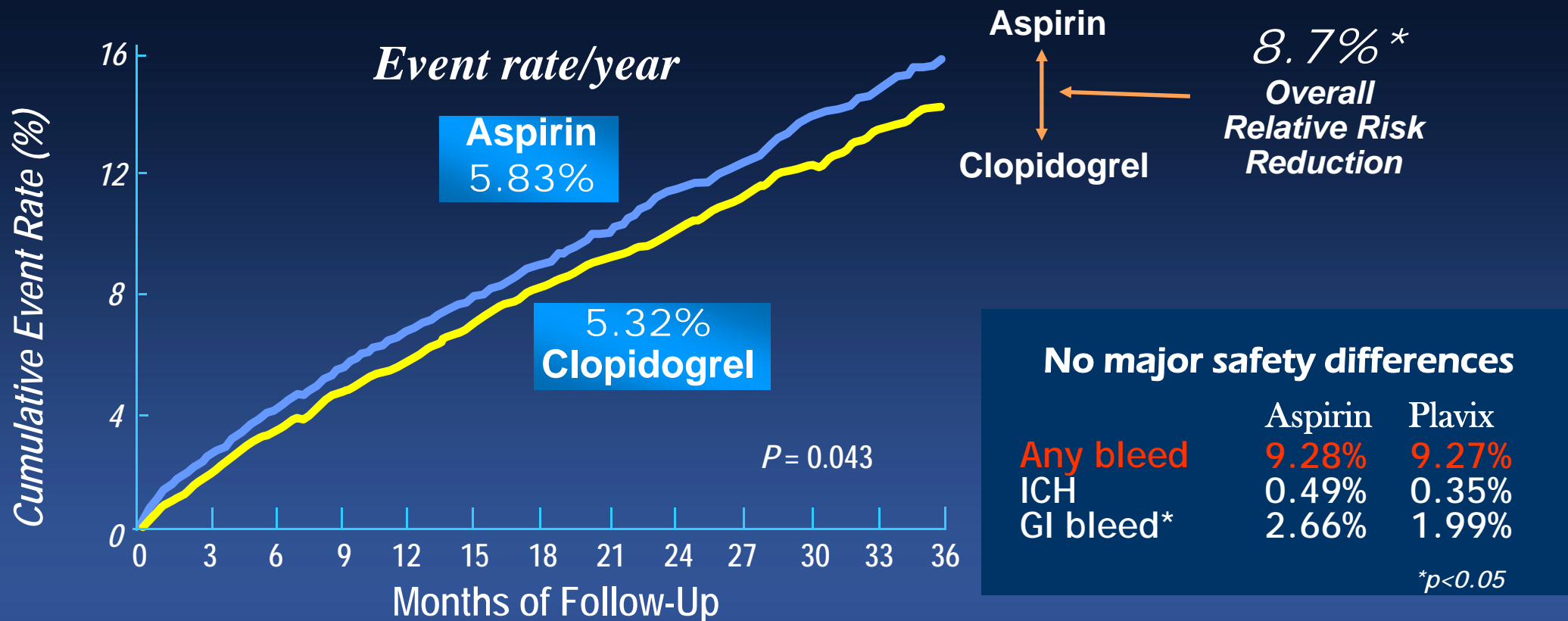
P2Y₁₂ Receptor

Platelet Activation Mechanisms

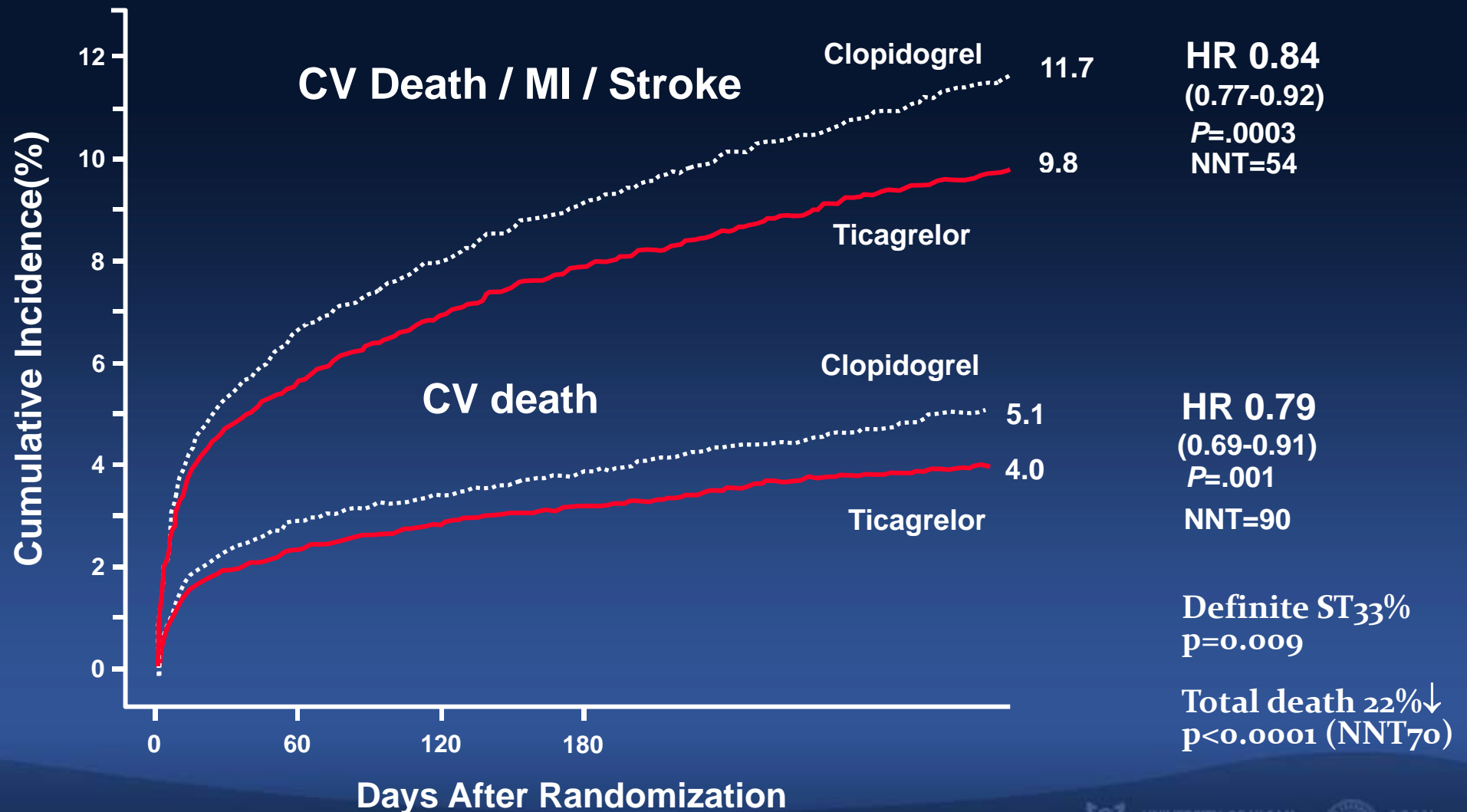


Cumulative Risk of Stroke, MI or Vascular Death in Patients in the CAPRIE Trial

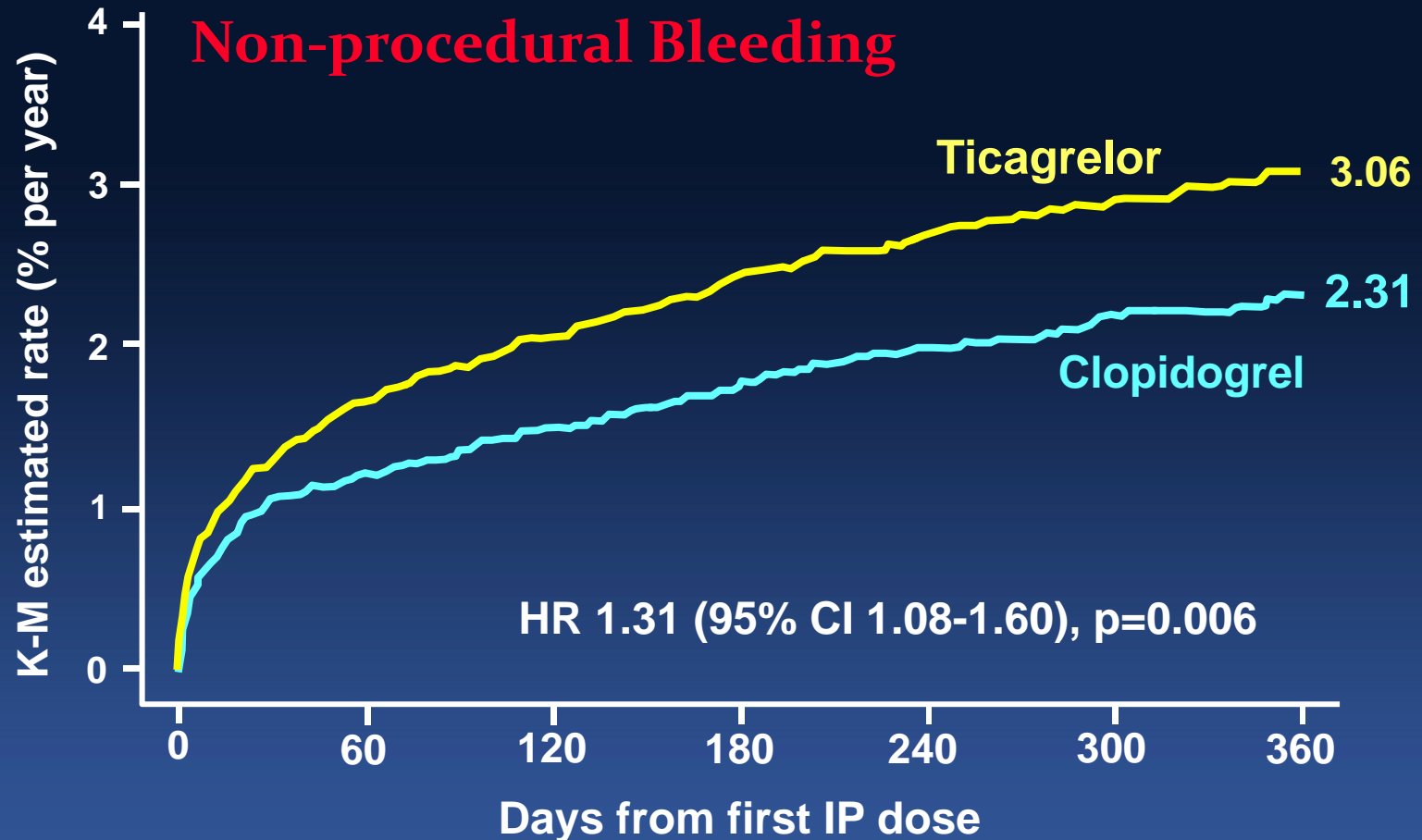
19,185 patients with atherosclerotic disease



PLATO: Major Outcomes



Bleeding Tax



No. at risk

Ticagrelor 9,235 7,641 7,247 6,979 5,496 4,067 3,698

Clopidogrel 9,186 7,718 7,371 7,134 5,597 4,147 3,764

“More Bleeding = More Death”

Impact of Bleeding on Mortality after PCI

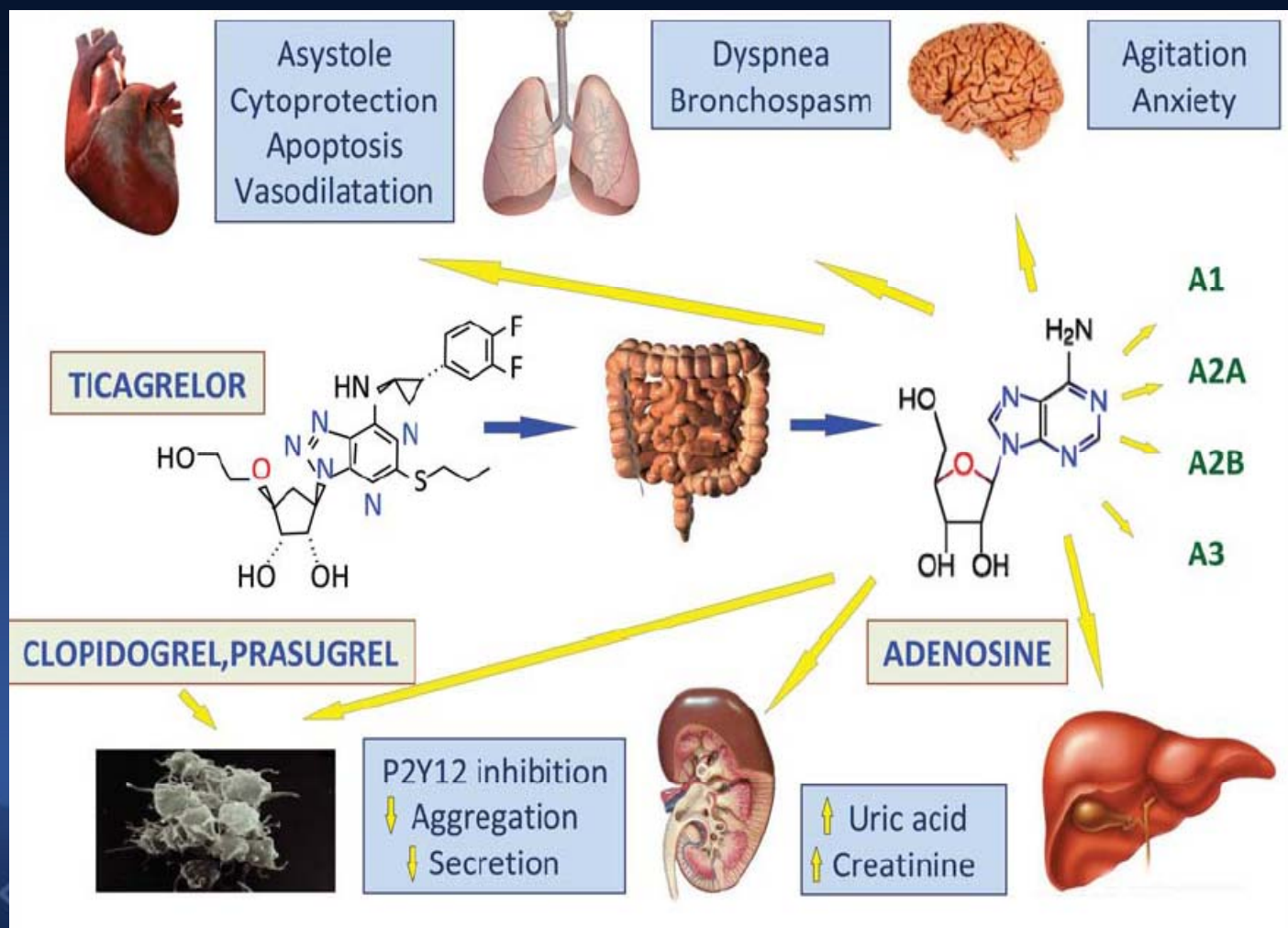
17,393 patients from REPLACE-2, ACUTY and Horizons



Adjusted Risk for 1-Year Mortality

The PLATO trial: do you believe in magic?

Victor L. Serebruany^{1*} and Dan Atar²



Adenosine Hypothesis ?

- vasodilation
- preconditioning
- immunomodulation
- dyspnea
- heart block
- renal function

Differential Expression of P2Y₁₂ Receptor in Culprit Plaques from Patients with AMI & Stable Angina

Am J Cardiol 2011 (in press)

We compared the expression of P2Y₁₂ receptors in coronary atherectomy tissues retrieved from 54 patients with AMI (n=35) or stable angina (n=19).

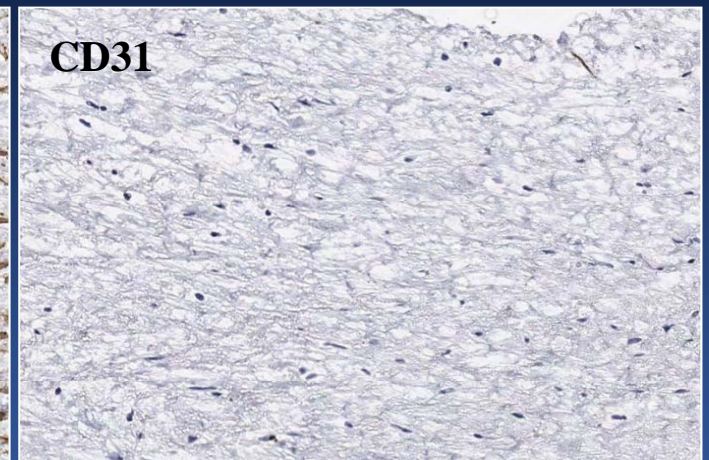
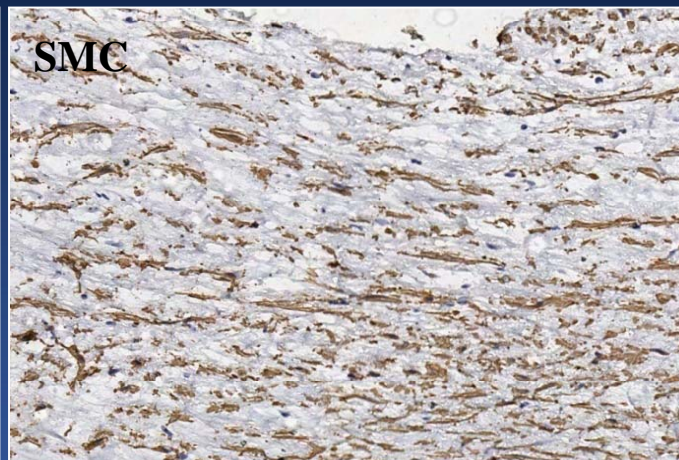
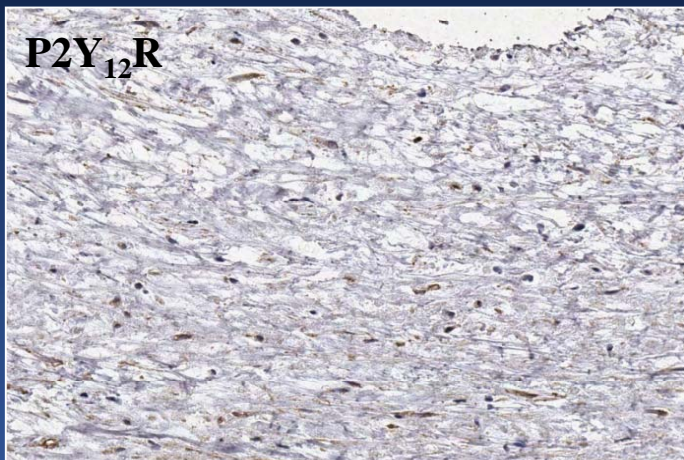
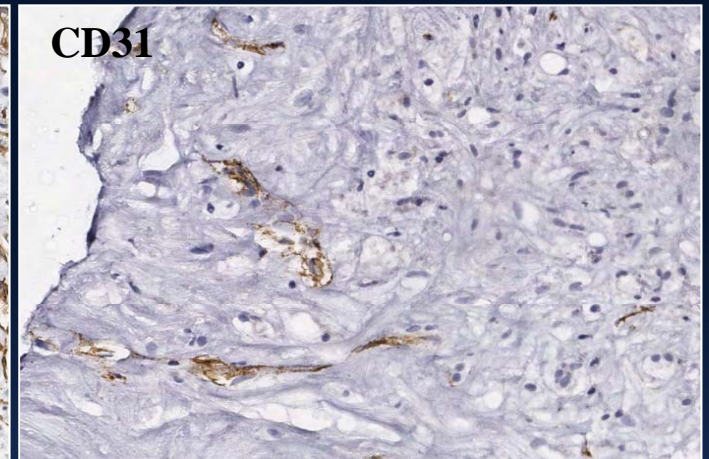
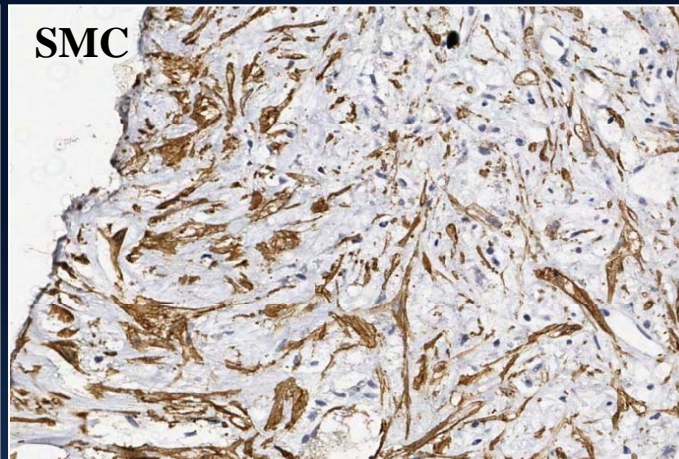
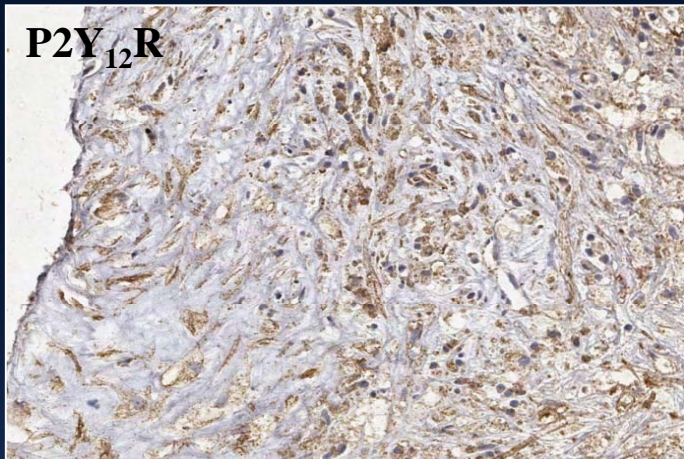
Immunohistochemistry

	AMI (n=35)	Stable angina (n=19)	<i>p</i> - value
α -SM actin (%)	2.9 \pm 2.7	12.3 \pm 14.4	0.011
CD31 (%)	1.1 \pm 1.6	0.2 \pm 0.2	0.001
CD68 (%)	15.5 \pm 13.6	7.0 \pm 14.6	0.038
P2Y12 Receptor (%)	1.1 \pm 0.9	0.5 \pm 0.4	<0.001

Data are shown as % positive area (immunostaining area/total plaque area \times 100).

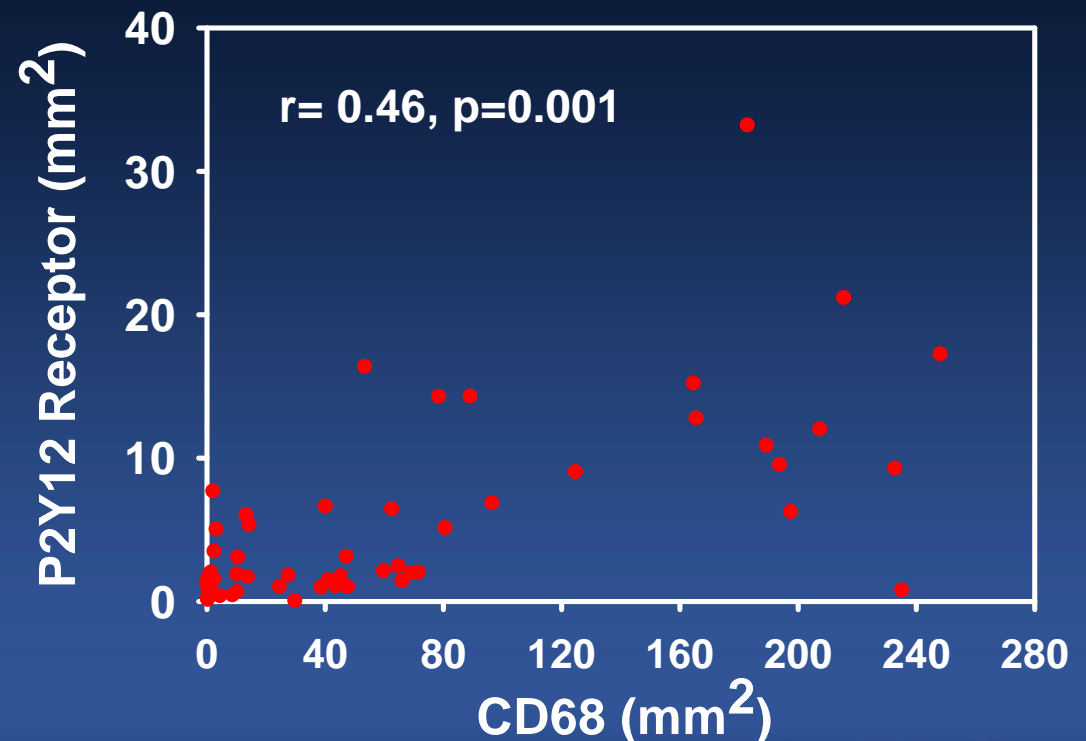
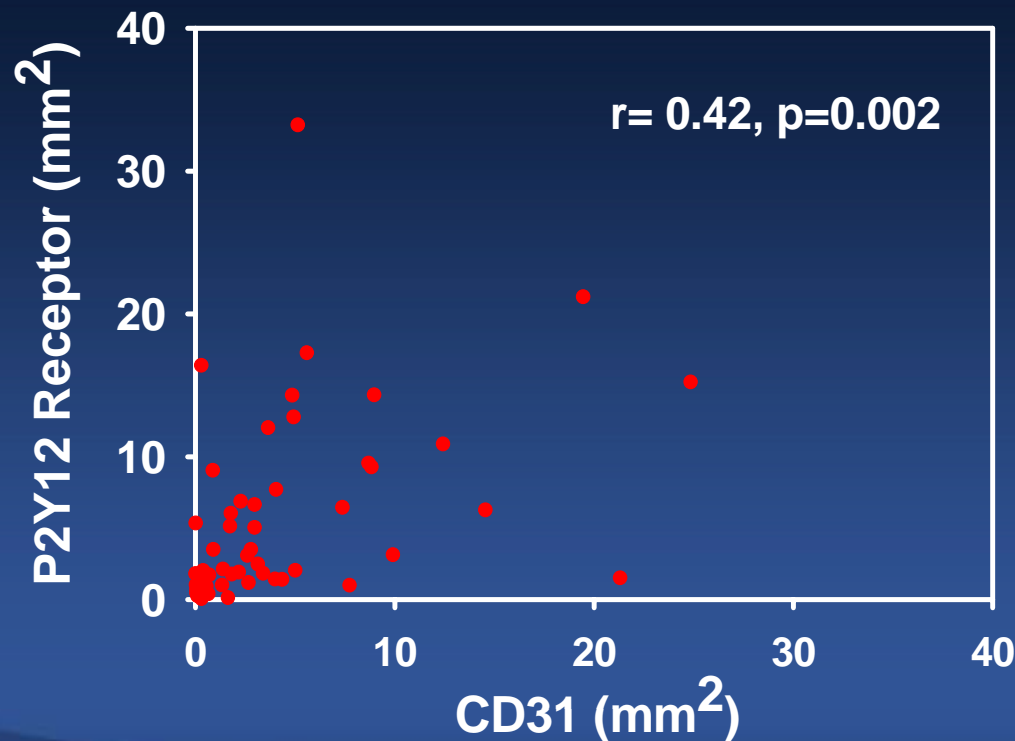
AMI: STEMI 27, NSTEMI 8

AMI

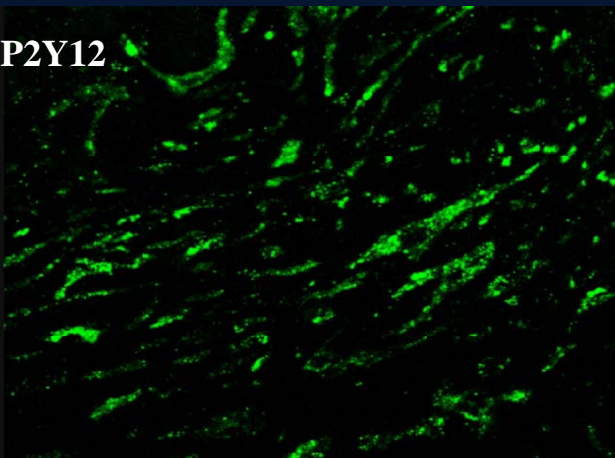


Stable angina

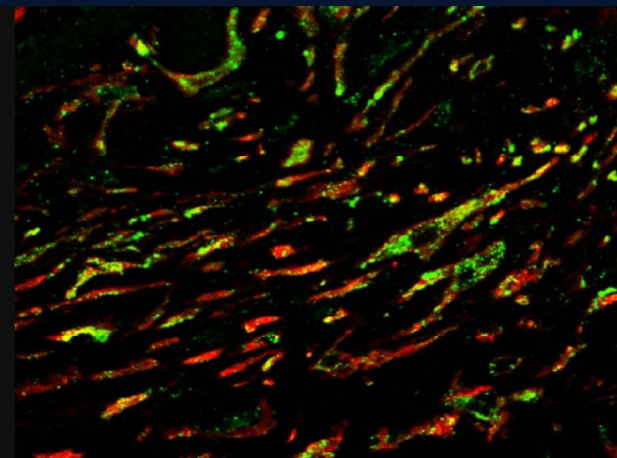
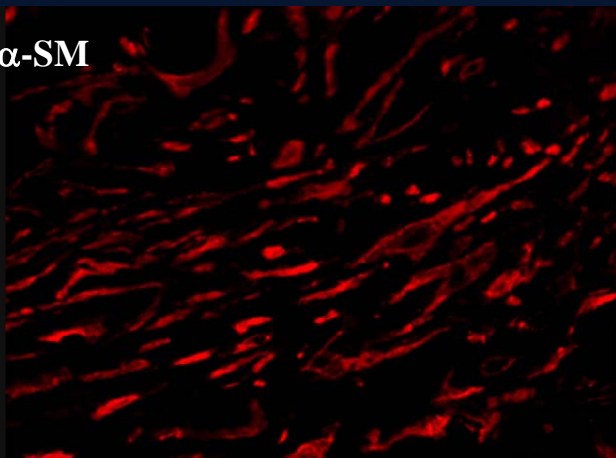
Relationship Between P2Y₁₂ Receptor-Positive Areas and CD31 or CD68-Positive Areas (mm²)



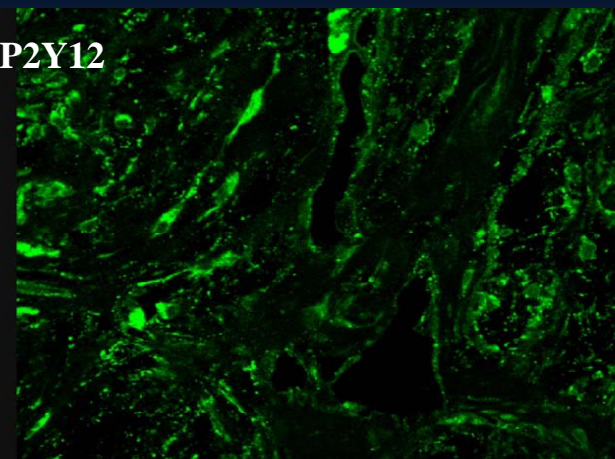
P2Y12



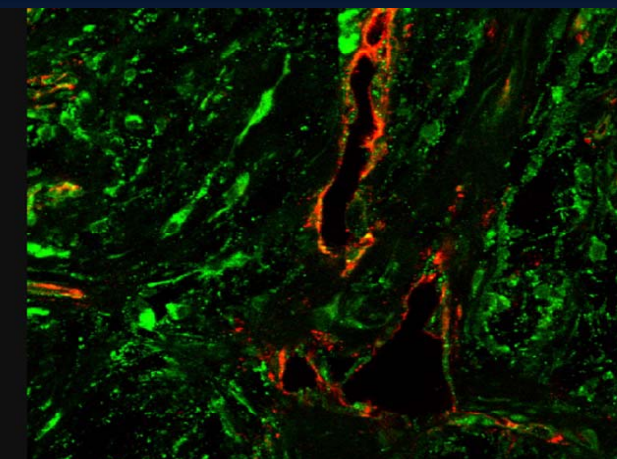
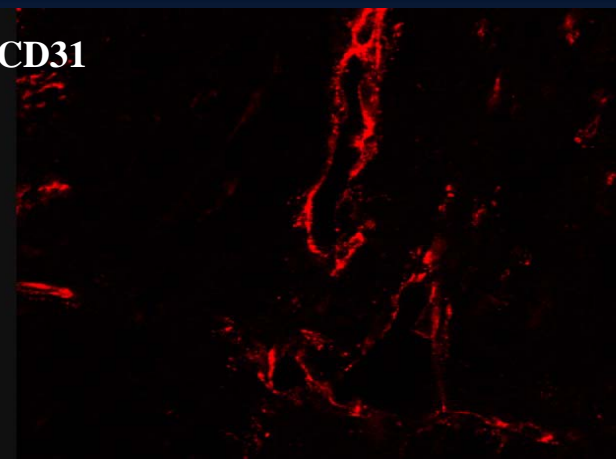
α -SM



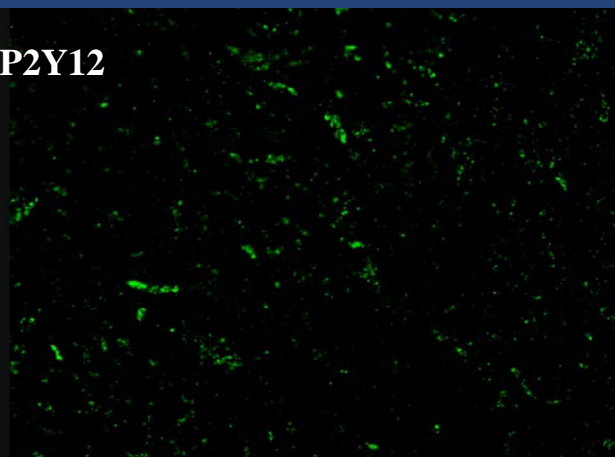
P2Y12



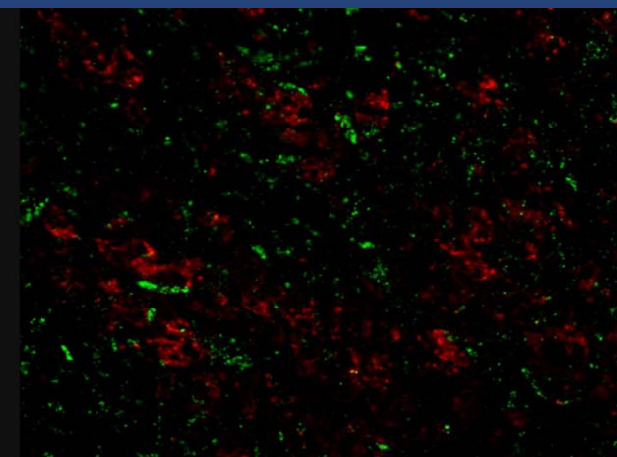
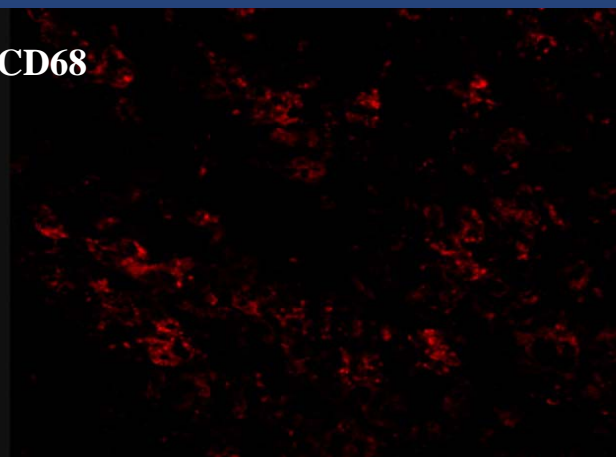
CD31



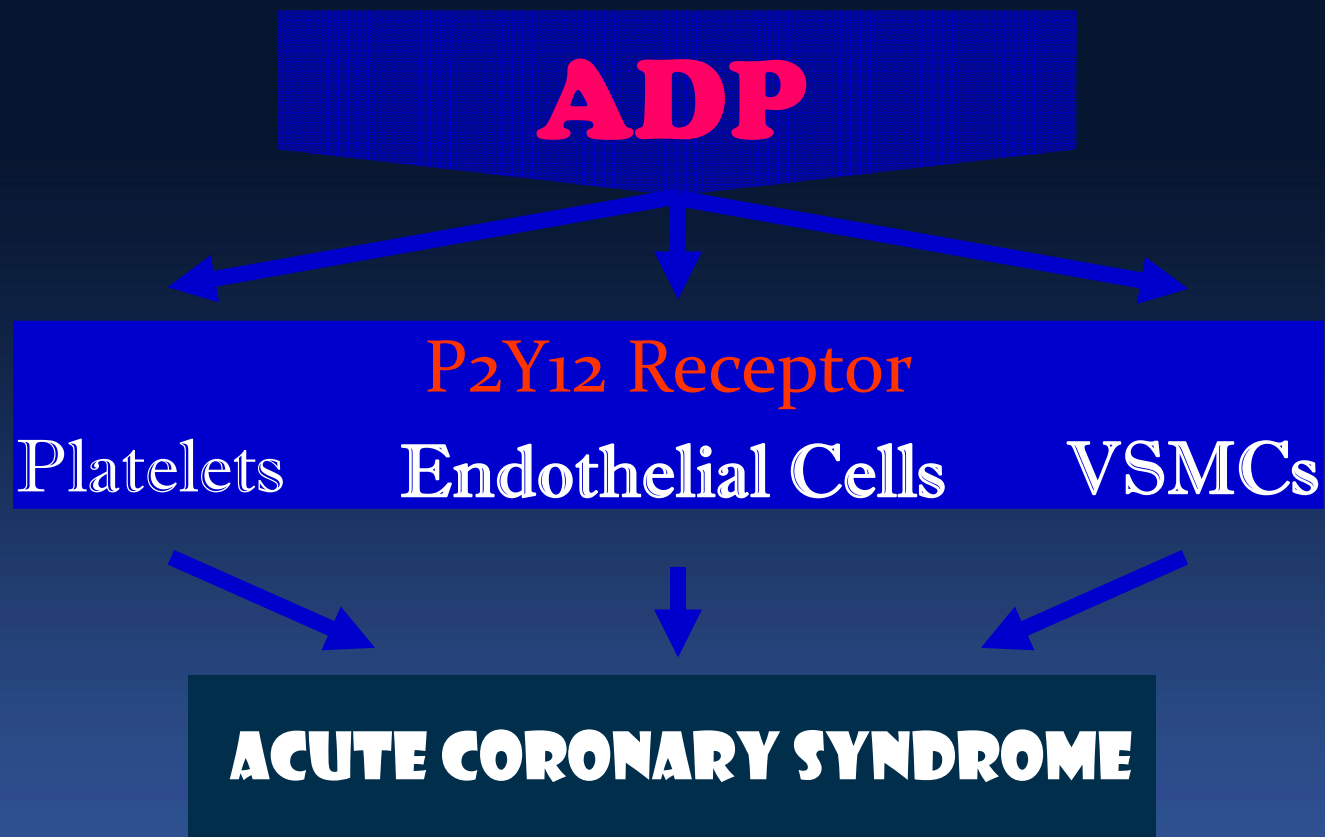
P2Y12



CD68



Summary



P2Y₁₂ receptor inhibitors may have a dual anti-ischemic effect by inhibiting both platelet activation and plaque destabilization.

Limitations

Specimens were obtained from selected lesions in large vessels because calcified, tortuous, small vessels & those with heavy thrombotic lesions are not suitable for DCA. Thus, our findings may not be applicable to other lesions in AMI patients.

It remains uncertain whether P_2Y_{12} R is a cause or consequence of plaque instability. You can see firefighters at every flaming building, but they did not set the blazes!

Thank You!

← ...looking for burning plaques

People start life with clean arteries,
live with atherosclerosis and
die of acute vascular events.

감사합니다.